tient. I do not think we should compare surgery performed in Canada to that in developing countries.

In any setting we should try to provide the best possible care. I have ethical concerns about performing an inferior procedure with inferior results on the basis that it is better than no surgery at all.

K.G. Romanchuk, MD, FRCSC
Professor and head
Department of Ophthalmology (Eye Centre)
University of Saskatchewan
Saskatoon, Sask.

On attending a microsurgery course Dr. Loosmore discovered that he did not possess the skills to suture with hair-thin materials and tiny needles. He proposes that young women with steady hands and good eyes be trained to perform this delicate task.

These well-trained women exist. They are today's surgeons! Why should they be paid less than those who cannot perform such tasks?

History reveals the opposite. In many fields (e.g., ballet, hockey and even medicine) those possessing superior technical skills have been most highly prized and valued. Perhaps surgeons who cannot perform highly technical skills should receive less remuneration than those who can.

As for his view of ophthalmic surgery, Loosmore needs to visit an ophthalmologic operating room, where he would learn that "the standard eye operations" are indeed technically difficult and demanding. Modern ophthalmologists routinely use the materials and techniques Loosmore confesses he cannot. Fortunately Loosmore did not choose a career in ophthalmology; he would be unable to perform the essential skills and keep up with the rapid technologic change in the field.

Patients subjected to crude cataract procedures performed by the teenage children of missionaries have no choice. I suspect that Loosmore, like any other Canadian, would want highly technical and successful cataract surgery for his eyes. If he ever needs cataract or other ophthalmic surgery I urge him to consult a well-qualified ophthalmologist. Furthermore, he should spend less time musing about the value and practice of technically skilled surgeons and more time upgrading his skills to become more valuable to his patients.

Pamela Velos, MD, FRCSC
Weston, Ont.

It is curious that Dr. Loosmore, after experiencing difficulty in a microsurgical course, decided that intraocular surgery is not technically difficult and could be better performed by technicians.

Fortunately for Canadian patients, the modern cataract-removal technique of phacoemulsification does not resemble the procedures done in missionary camps. It requires a high level of technical skill and the identification and prevention of complications. The remarkable results are due more to the training and dedication of the surgeons than to the simplicity of the procedure.

It is disturbing that Loosmore's experiences of surgical problems and leaking anastomoses have led him to form such a low opinion of others' abilities. If he is genuinely concerned with advancing patient care he would be well advised to research his material before offering his theories for publication in a national journal.

Carl V. Jones, BM
Vancouver, BC

[The author responds:]

I apologize if my article offended anyone; causing offence was not my intention. It is disturbing that one small paragraph of the short, obviously tongue-in-cheek article gave rise to a sustained tirade.

I do not trivialize surgery, and I have the greatest admiration for ophthalmologists and their abilities. In response to Dr. Spencer, to suggest that a general surgeon should try to fashion a water-tight wound in eye tissue is absurd. As Dr. Jones indicates, I have experienced the distress of a leaking anastomosis: what honest general surgeon with 35 years' experience, much of it in developing countries, would claim otherwise? I admit that I cannot perform microsurgery to my satisfaction, but I did not say that some eye operations could be better performed by technicians.

My article was intended to consider who might best carry out fine surgery, not to recommend a particular group. The unpleasant overreaction has the hyperbole of a second-rate soap opera. Perhaps my article on robots in surgery should wait awhile.

Brian Loosmore, MB, FRCS
Drayton Valley, Alta.

Intrapartum penicillin prophylaxis of early-onset streptococcal infection

In their article "Effectiveness of intrapartum penicillin prophylaxis in preventing early-onset group B streptococcal infection: results of a meta-analysis" (*Can Med Assoc J* 1993; 149: 1659–1665) Upton D. Allen, MB, BS, Lissette Navas, MD, and Susan M. King, MD, CM, conclude that intrapartum penicillin prophylaxis in women whose birth canals are colonized by group B streptococci is effective in preventing early-onset neonatal disease. Although their methods appear appropriate, we have some concerns.

Through a similar search strategy we identified relevant meta-analyses[1–3] and randomized controlled trials (RCTs)[4–9] the authors did not consider. Three of the studies they included were duplicate publications. Studies by Tuppurainen and Hallman,[6,10] Boyer and Gotoff,[4,11] and Morales, Lim and Walsh[5,12] were published during the recruitment of subjects and at trial completion. Between the first[4] and second[11] publications of the study by Boyer and

Gotoff, one of the authors stated, "In order to show efficacy in preventing GBS [group B streptococcal] disease, we need an additional case in our control group."[13] This indicates that the researchers had examined the data several times, increasing the probability of a type I error (rejecting the null hypothesis when it is true), and that they may have examined the control group more closely than the treatment group, increasing the risk of diagnostic suspicion error.

Allen, Navas and King use invasive neonatal GBS infection as the primary outcome, but they do not define it. One neonate with bacteremia but no symptoms of sepsis[11] and several neonates with a positive urine latex agglutination test result but a negative result from central blood culture[10,14] were considered to have invasive infection. The urine latex agglutination test is not reliable,[15] yet it was used to diagnose infection in the two studies that showed a significant decrease in the rate of infection among treated neonates.[10,14] Blood or urine samples were more likely to have become contaminated in the control group than in the treatment group, in which GBS surface colonization was reduced by intrapartum chemoprophylaxis.

In calculating the odds ratios (ORs) the authors use the number of infants with invasive disease as the numerator and the number of mothers as the denominator. We feel that the denominator should have been the total number of infants, to account for multiple births.

Boyer and Gotoff[11] administered ampicillin every 12 hours to all infants in the treatment group until culture results were available but treated only infants with symptoms in the control group. This intervention may have reduced the GBS infection rate in the treatment group; therefore, it is incorrect to combine this study with others in which antibiotics were administered intrapartum only.

Although there is no gold standard for assessing the quality of an RCT, the method used by Allen, Navas and King is suspect; a nonblinded, nonrandomized trial in which the baseline comparison of groups was not mentioned and in which 80% or less, or an unknown percentage, of randomized patients were followed would still have a score of 0.25. We assessed three of the RCTs in their study using a method described by Chalmers and associates,[16] in which the degree of blinding is considered the most important aspect of any trial, and we obtained quality scores of 0.19,[17] 0.38[10] and 0.50.[11] Although the ranking is the same as that obtained by Allen, Navas and King, their scores are higher (0.58, 0.67 and 0.71 respectively).

Another of the studies violated the randomization process by assigning patients allergic to ampicillin to the control group[12] and thus should not have been included in the meta-analysis.

In all of the studies there was a risk of diagnostic suspicion bias (when knowledge of a patient's treatment may influence the intensity and the outcome of the diagnostic process) because neonates were not assessed by a blinded investigator. This lack of blinding is critical because none of the studies had standardized follow-up procedures.

Boyer and Gotoff[11] excluded patients after randomization owing to intrapartum fever, randomization errors and incomplete data. This resulted in an overall dropout rate of 11%, which is not justifiable in a hospital-based study with short-term outcomes.[16]

We consider it inappropriate to include these trials in a meta-analysis because of flaws in their methods. "An overview which incorporates low-quality studies is worse than useless, for it may mislead."[18]

Arne Ohlsson, MD, MSc, FRCPC
Terri L. Myhr, MSc
University of Toronto Perinatal
Clinical Epidemiology Unit
and the Department of Newborn
and Developmental Pediatrics
Women's College Hospital
Toronto, Ont.

References

1. Wang E, Smaill F: Infection in pregnancy (Group B streptococcus). In Chalmers I, Enkin M, Keirse MJN (eds): *Effective Care in Pregnancy and Childbirth*, Oxford University Press, Oxford, England, 1989: 551–555
2. Smaill F: Intrapartum antibiotics for group B streptococcal colonisation. [article] In Chalmers I (ed): *Oxford Database of Perinatal Trials* (version 1.3, disk issue 7), Oxford Electronic Publishing, Oxford University Press, Oxford, England, 1992; Spring (record 3006)
3. Baley JE, Fanaroff AA: Neonatal infections. Part 2: Specific infectious diseases and therapies (2. Group B streptococcal infections). In Sinclair JC, Bracken MB (eds): *Effective Care of the Newborn Infant*, Oxford University Press, Oxford, England, 1992: 480–483
4. Boyer KM, Gadzala CA, Kelly PD et al: Selective intrapartum chemoprophylaxis of neonatal group B streptococcal early-onset disease. III. Interruption of mother-to-infant transmission. *J Infect Dis* 1983; 148: 810–816
5. Lim DV, Morales WJ, Walsh AF et al: Reduction of morbidity and mortality rates for neonatal group B streptococcal disease through early diagnosis and chemoprophylaxis. *J Clin Microbiol* 1986; 23: 489–492
6. Tuppurainen N, Österlund K, Hallman M: Selective intrapartum penicillin prophylaxis of early-onset group B streptococcal disease. [abstr] *Pediatr Res* 1986; 20: 493A
7. Omeñaca Teres F, Matorrás JR, García-Perea A et al: Prevention of neonatal group B streptococcal sepsis. [C] *Pediatr Infect Dis J* 1987; 6: 874
8. Matorrás JR: *Colonización materna por* Streptococcus *del grupo B (SGB): profilaxis de la sepsis neonatal* [doctoral thesis], Universidad Autonoma Madrid, Madrid, 1986
9. Matorrás R, García-Perea A, Madero R et al: Maternal colonization by group B streptococci and puerperal infection; analysis of intrapartum chemoprophylaxis. *Eur J Obstet Gynecol Reprod Biol* 1991; 38: 203–207
10. Tuppurainen N, Hallman M: Prevention of neonatal group B streptococcal disease: intrapartum detection and chemoprophylaxis of heavily colonized parturients. *Obstet Gynecol* 1989; 73: 583–587
11. Boyer KM, Gotoff SP: Prevention of early-onset neonatal group B streptococcal disease with selective intrapartum chemoprophylaxis. *N Engl J Med* 1986; 314: 1665–1669
12. Morales WJ, Lim DV, Walsh AF: Prevention of neonatal group B streptococcal sepsis by the use of a rapid screening test and selective intrapartum chemoprophylaxis. *Am J Obstet Gynecol* 1986; 155: 979–983
13. Gotoff SP: Chemoprophylaxis of early

For prescribing information see page 1329 →

onset group B streptococcal disease. *Pediatr Infect Dis J* 1984; 3: 401–403
14. Morales WJ, Lim D: Reduction of group B streptococcal maternal and neonatal infections in preterm pregnancies with premature rupture of membranes through a rapid identification test. *Am J Obstet Gynecol* 1987; 157: 13–16
15. Sanchez PJ, Siegel JD, Cushion NB et al: Significance of a positive urine group B streptococcal latex agglutination test in neonates. *J Pediatr* 1990; 116: 601–606
16. Chalmers TC, Smith H, Blackburn B et al: A method for assessing the quality of a randomized control trial. *Controlled Clin Trials* 1981; 2: 31–49
17. Matorrás R, García-Perea A, Omeñaca F et al: Intrapartum chemoprophylaxis of early-onset group B streptococcal disease. *Eur J Obstet Gynecol Reprod Biol* 1991; 40: 57–62
18. Cook DJ, Guyatt GH, Laupacis A et al: Rules of evidence and clinical recommendations on the use of antithrombotic agents. *Chest* 1992; 102 (suppl 4): 305S–311S

[Two of the authors respond:]

The issues Dr. Ohlsson and Ms. Myhr raise strengthen the conclusions of our study.

The related meta-analyses from the Oxford perinatal database,[1-3] which we used to identify studies in progress but not meta-analyses, used different summation procedures from ours but also suggested a favourable effect of intrapartum penicillin in preventing early-onset GBS infection.

We identified the six RCTs Ohlsson and Myhr cite.[4-9] They included a study addressing the effect of intrapartum prophylaxis on puerperal infection instead of early-onset disease,[4] a letter to the editor[5] and a related thesis,[6] an abstract[7] and two interim reports.[8-9] The results of the studies addressing early-onset GBS infection[5-9] were all published on completion of the studies,[10-13] and the final publications are included in our meta-analysis.

Our analysis is not affected by whether Boyer and Gotoff[11] examined their data several times, thus increasing the chance of a type I error, without adjusting their significance level.[14] Our calculations are based on raw data and are not affected by *p* values. Whether these researchers examined the control group more closely after interim analysis is speculation.

Although our definition of invasive disease was not published, we defined it as a positive culture result from blood or cerebrospinal fluid (CSF) samples, soluble antigen in CSF or urine in the presence of clinical evidence of GBS infection, or a positive culture result from postmortem samples taken from previously sterile sites. In the study by Boyer and Gotoff[11] the neonate with bacteremia but no obvious symptoms of sepsis would be regarded as having invasive GBS infection, particularly because the infant was one of five born to mothers at high risk of transmitting GBS infection, given that labour was premature (which may be a symptom of GBS infection) and that there was prolonged rupture of membranes. The natural course of untreated asymptomatic bacteremia is likely to be metastatic infection (especially meningitis), fulminant disease and death.[15]

With respect to the two studies that used latex agglutination tests, Morales, Lim and Walsh[12] stated that "neonatal sepsis was diagnosed on the basis of positive results of body fluid cultures." Although Tuppurainen and Hallman[10] used the latex agglutination test, they did not indicate that a positive result was part of their diagnostic criteria for early-onset GBS infection. Their criteria were severe symptoms (including respiratory distress and signs of shock within 48 hours after birth), a positive culture result from blood samples or presence of group B streptococci in superficial cultures, and leukopenia or elevated C-reactive protein level.

We calculated ORs using the number of infants as well as the number of mothers as denominators; because these denominators differed only slightly, the results were almost identical (common OR 0.03, 95% confidence interval [CI] 0.0013 to 0.17). However, we felt that the number of infants was a less reliable denominator because data on multiple pregnancy were available from only three of the seven studies in our meta-analysis.[11-13] In the remaining studies[10,12,16,17] the number of births and mothers appeared to be the same, but this would need to be verified.

Ohlsson and Myhr appear to have misinterpreted the outcome measure in the study by Boyer and Gotoff.[11] The authors examined the effect of intrapartum chemoprophylaxis on bacteremia by taking blood samples for culture at birth; thus, postnatal administration of antibiotics would not affect this outcome measure. Even if this study were removed from the meta-analysis the pooled OR of the remaining RCTs would still show a beneficial effect of penicillin (OR 0.06, 95% CI 0.003 to 0.49).

Ohlsson and Myhr concur with us that there is no gold standard for assessing the quality of an RCT. We are pleased that our method was explicit enough that they could easily follow it and compare it with another, which yielded a similar ranking. With respect to the nonblinded, nonrandomized example given by them, we agree that a rating of 0.25 (out of a maximum of 1) does not suggest a high-quality study.

We agree that the assignment of patients allergic to ampicillin to the control group in one study violated randomization.[12] The importance of such a systematic bias depends on its effect on the results. There is no known biologic reason to expect women allergic to ampicillin to be at greater risk of delivering infants with GBS infection and, therefore, no reason to believe that the study would have had more cases of GBS infection in the control group.

It is well recognized that a lack of blinding introduces a risk of diagnostic suspicion bias;[18] however, a careful examination of each study shows the potential effect of this bias on the results. For example, in the study by Boyer and Gotoff[11] if single standard blood samples were taken from all infants at birth to culture for bacteremia, this bias would be less relevant. Thus, although blinding is important, its effect in re-